REMARKS

The final Office action dated February 24, 2003 is acknowledged. Claims 1, 3-9 and 11-15 are pending in the instant application. According to the Office action, each of those claims have been rejected. By the present "Reply to Final Office Action," claims 1 and 15 have been amended. Reconsideration is respectfully requested in light of the amendments being made hereby and of the following remarks.

Objection to Claim 1

The Examiner has objected to claim one because the word "is" was included at the end of line 6 inappropriately. The word has been deleted from the claim and Applicant respectfully requests that this objection be withdrawn.

Rejection of Claims 1, 3-9 and 11-15 under 35 U.S.C. 103(a)

Claims 1, 3-9 and 11-15 have been rejected as being unpatentable over U.S. Patent No. 5,683,711 (Fischer et al.) in combination with U.S. Patent No. 4,954,343 (Hosaka et al.). It is respectfully submitted that these claims in their present form are patentably distinct from the prior art.

The Examiner states that Fischer discloses a transdermal patch comprising estradiol and norethisterone in a supersaturated state in adhesive matrix and the viscosity of the adhesive matrix can inhibit crystallization of the supersaturated adhesive. In addition, the Examiner states that the adhesive comprises acrylate polymers, such as butyl methacrylate and dimethylaminoethyl methacrylate. The Examiner notes that this reference does not teach butyl methacrylate and dimethylaminoethyl methacrylate as crystallization inhibitors.

However, the reference does teach, according to the Examiner, that the high viscosity of the adhesive inhibits the crystallization, according to the Examiner.

The Examiner additionally states that Hosaka teaches a dermal pharmaceutical preparation comprising a pressure sensitive adhesive comprising methacrylate having an amino group to maintain the drug in a dissolved state and inhibits crystallization. The Examiner points out that examples of the amino containing adhesive include methyl methacrylate and examples of the drug to be delivered by this formulation are progesterone and estradiol, used individually or in combination in an amount of 0.1 to 30%. The Examiner further states that the adhesive layer has a support layer and has a thickness of 5 to 1000 micrometers.

It is the Examiner's contention that it would have been obvious to one having ordinary skill in the art at the time the invention was made to obtain a transdermal drug delivery device according to Fischer comprising steroid hormones and PSA wherein the steroids are in supersaturated concentration and replace the PSA with the amino group containing polymers of Hosaka, with the reasonable expectation of success of inhibiting crystallization of the drug in the transdermal drug delivery device. The Examiner has the opinion that motivation therefor would arise from the teaching of Hosaka that the amino-group containing polymer maintains the drug in dissolved state and provides excellent drug liberation and adhesion to the skin.

Applicant respectfully disagrees and submits that the present invention is a transdermal therapeutic system in plaster form for the controlled release of estradiol and norethisterone, wherein the reservoir layer is prepared using polyacrylate pressure-sensitive

adhesives and further contains a crystallization inhibitor. Applicant emphasizes that the polyacrylates of the pressure-sensitive adhesive for the plaster of the present invention do not contain amino groups. Applicant respectfully submits that this feature of the polyacrylates not containing amino groups would be apparent to one skilled in the art and would be easily inferred from the specification on the whole. For example, the examples of the specification of the present invention provide for Durotak 387-2287, which one skilled in the art would surely recognize as being a pressure-sensitive polyacrylate adhesive not containing amino groups. Applicant points out that claim 1, as amended, reflects this feature of the present invention.

Applicant also submits that claim 1 was amended to delete "...and a copolymer based on butyl methacrylate, 2-dimethylaminoethyl methacrylate and methyl methacrylate being present in a molar ratio of 1:2:1 (butyl methacrylate : 2-dimethylaminoethyl methacrylate : methyl methacrylate)" from the list of inhibitors. As amended, claim 1 more precisely recites that the present invention is a transdermal therapeutic patch for the administration of estradiol and norethisterone not comprising any amino group-containing polyacrylates. In contrast to the prior art, all amino groups of the present invention are provided by amino group-containing polymers other than acrylates. Applicant submits that such a patch was not obvious to one skilled in the art, that such a patch would not be inferred from either Fischer or Hosaka, alone or in combination, nor would it be obvious that amino-group containing polymers other than polyacrylates may serve as crystallization inhibitors for steroids.

With respect to the references cited by the Examiner, according to Fischer '711, it is due to the high viscosity of the adhesives that crystallization is inhibited. Alternatively,

Hosaka '343 solely teaches pressure-sensitive adhesives being a copolymer comprising a (meth)acrylate having an amino group as a co-monomer unit to provide a preparation which keeps the drug in a dissolved state. Hence, Applicant respectfully submits that the combined view of both references would only teach the use of a copolymer possessing a high viscosity and comprising a (meth)acrylate having an amino group as a co-monomer unit. As Applicant noted above, such preparations are specifically excluded from the scope of the present invention according to claim 1 as amended. Additionally, none of the aforementioned references teaches that copolymers or polymeric mixtures comprising a polyaminoamide, polyaminoimidazolidine, polyetherurethaneamine, polyamine or polyglucosamine may inhibit crystallization of the pharmaceutically active compound within the reservoir.

Applicant respectfully submits that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references when combined must teach or suggest all of the claim limitations (emphasis added). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on Applicant's disclosure (M.P.E.P. Sec. 706.02(j)). As noted above, neither reference, alone or in combination, teaches each and every feature of the present invention. It is therefore respectfully requested that the application defined in the claims is patentably distinguishable over the art under 35 U.S.C. 103(a).

Conclusion

For the foregoing reasons, it is respectfully submitted that the present application is in condition for allowance, and such action is earnestly solicited. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

By: _____
D. Peter Hochberg

D. Peter Hochberg Co., L.P.A.
1940 E. 6th St. – 6th Floor
Cleveland, OH 44114-2294
(216) 771-3800